IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant	:	Weber, Eckard, et al.
Appl. No.	:	10/828,795
Filed	:	4/21/2004
For	:	COMPOSITIONS FOR AFFECTING WEIGHT LOSS
Examiner	:	Zhang, Nancy L.
Group Art Unit	:	1614

DECLARATION OF MICHAEL A. COWLEY, Ph.D., UNDER 37 CFR §1.132

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

I, Dr. Michael A. Cowley, declare and state as follows:

1. I am a co-founder, shareholder, and Chief Scientific Officer to Orexigen Therapeutics, Inc., which is the assignee of the above-captioned application. I am also a co-inventor of the invention disclosed in the instant application.

2. My scientific Curriculum Vitae, including my list of publications, is attached to and forms part of this Declaration (Exhibit A).

3. I am an expert in the field of the invention, and am an inventor listed on numerous patent applications related to the treatment of obesity. I have extensive knowledge regarding the subject matter of the above-captioned application, including the clinical trials discussed in more detail below.

4. The claimed subject matter of the above-captioned application relates to compositions and methods for affecting weight loss comprising naltrexone and bupropion. Orexigen, the assignee of the instant application, has conducted a Phase II and a Phase IIb clinical trial of the combination of naltrexone and bupropion ("Contrave") to treat obesity. The protocols and results of these clinical trials are accurately reported in Appendix B attached hereto, which forms a part of this declaration.

5. Of particular relevance are the following results: Among completers of the Phase II trial, at 16 weeks Contrave demonstrated mean weight loss of 4.8% of baseline body weight, compared to 3.9 % for bupropion alone, 2.3% for naltrexone alone and 1.0% for placebo. One important observation in this trial was that the benefit of adding naltrexone became more apparent over time, as weight loss curves for the combination therapy group gradually diverged

from the bupropion monotherapy group, and by 24 weeks, Contrave showed 6.8% weight loss, compared to 4.5% for bupropion alone. In the Phase IIb trial, all three dosages of Contrave tested were significantly better than either of the monotherapies when comparing mean weight loss among completers at 24 weeks. In addition, for the completer population of the Phase IIb trial, between 64% and 70% of patients on the three dosages of Contrave lost at least 5% of their body weight, compared to 32% for bupropion alone, 15% for naltrexone alone and 20% for placebo. Between 24% and 32% of patients on the three dosages of Contrave in the completer group lost at least 10% of their body weight, compared to 9% for bupropion alone, 3% for naltrexone alone and 3% for placebo.

6. The results of the clinical studies reported in detail in Appendix B are surprising and unexpected in light of what was known in the field at the time of filing of the instant application. The results clearly demonstrate that the combination of naltrexone and bupropion has unexpected and non-obvious properties in comparison to the individual components.

7. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information or belief are believed to be true, and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful statements may jeopardize the validity of the application or any patent issued thereon.

By: _____ Date: 1/19/07

Michael A. Cowley, Ph.D.

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